Problems with the dissemination of up-to-date information on the results of endograft repair for abdominal aortic aneurysm

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The article entitled "Periprosthetic leak and rupture after endovascular repair of abdominal aortic aneurysm: The significance of device design for long-term results" by Krohg-Sørensen et al and the invited commentary by Zarins in this issue bring up a serious concern regarding endograft repair of abdominal aortic aneurysms (AAA)—namely, the problem of obtaining up-to-date and complete information on the performance of the devices that are undergoing clinical trial. Of particular concern is that a major part of this problem may be related to the control of trial data by industry.

The delay between completion of a study, analysis of the data, and submission and publication of the manuscripts may be considerable. Consequently, the practicing surgeon may lack information to guide safe and proper patient management. Even those surgeons not directly involved in this new technology need this information to determine the best current management for their patients with AAA and to possibly refer those patients for endograft repair or enlist them into a particular trial. This delay in release of information is understandable in blinded randomized drug trials but should not be a problem in the trials of AAA endograft devices, which cannot be blinded and which, up to now, have not been randomized. Data are being collected steadily, and information is potentially available throughout all phases of these trials. This should be straightforward if a data monitoring committee is provided with information, including complications, on a regular basis. It is just a matter of what information is disseminated and how and of how frequent and complete the reports are. Let us look at what has happened so far in this new field.

First, there has been a tendency to "hype" this new technology from the beginning. It is natural for both the primary investigators and the company to want others to share their enthusiasm for the new technology. In early presentations of the data at conferences and symposia, the unlikelihood of being held responsible for what is said, as compared with what is printed in a submitted manuscript, encourages speculative claims that the subsequent data may not support. With the numerators and denominators changing quickly with each update, it has been difficult for those not intimately involved in these trials to develop an accurate perspective on mortality and major morbidity rates, the rate and fate of endoleaks, etc. However, because the data should be collected in such a way to be suitable for publication, there is no reason why full and accurate reports of nonproprietary information cannot or should not be regularly presented at such meetings and symposia, with objective reporting practices, just as one would at a national or regional society meeting where the paper is discussed and peer reviewed. This would reduce much of the unfounded speculations and misleading impressions that have characterized many of the early presentations of these new devices.

At the beginning, particularly in the active patient recruitment phase, information is usually readily obtained as data from investigator's meetings are allowed to be presented elsewhere by them. Later, it is common practice that only "official" data releases are allowed. Sometimes, as happened with Endovascular Technologies (EVT), restrictions on data release are explained by the need for compliance with inside trader rules, if the company has gone public, but when

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The author was a principal investigator and served on the Scientific Advisor Board of Endovascular Technologies (EVT) up until the completion of phase I of its trial and informally consulted (without compensation) with the EVT's medical director on occasion after that.

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information available outside investigator's meetings is limited to periodic press releases, which amount to limited views of outcome data intended more for investors than investigators, scientific progress and integrity is not being served. If periodic open and uniform release of data is the avowed goal (to comply with inside trader rules), there is no reason, outside of the obvious self-serving one, that the data released cannot be full and complete and the intervals reasonably frequent. The details of the device and its deployment are indeed proprietary, and objective data from a clinical trial should not be so considered. The principle investigators and the company should feel a responsibility to do this.

Eventually, publications begin to appear—often multiple publications on each device. It is understandable if multiple publications arise during a long three-phase trial of a new device. One of the problems with multiple publications of the same longitudinal data is that subsequent accounts may have different starting points, ostensibly because the device itself, or the deployment system, has undergone redesign and reengineering and with the understandable intent that the method gets full credit for such improvements. However, this practice also hides the learning curve. The "hook breaks" may have seemed like a disaster to the EVT trial, and potentially were, but now reporting only data since the trial recommenced in November 1995 has been a blessing. It is not that it is inappropriate to show the effect of improvements in the device or the skills of those implanting it but that it is more appropriate to present the entire experience and make those points by subgroup analysis and let the reader be the judge.

Unfortunately, it appears that some of those investigators who present data on company-sponsored clinical trials have not been close to the data collection or analysis and have not performed or checked the statistical analyses. In some cases, they have not been able to supply key additional information requested by discussants or reviewers. Having the data primarily handled by the company and analyzed by it has other potentially serious drawbacks. The main reason for regular, prompt, and complete disclosures of the outcomes of new devices is not so much to allow comparison of technical success rates, procedural mortality rates, and average length of stay in the hospital, the outcome criteria featured in most early reports because proper comparison necessitates long-term data. Rather it is to fulfill the need to assess the failure rates and major complications and their severity and impact, because ultimately, patient safety is at stake. This cannot be accomplished by carefully controlled releases of selected data intended to place the device in the best light. Even periodic investigator meetings may not fulfill this need when the data are prepared and presented by company officials or when the investigators are instructed not to disseminate the information.

Serious device complications, or design and fabrication flaws that can potentially lead to them, should be reported immediately rather than when it is apparent beyond reasonable doubt that the device is guilty of producing serious complications. Such was the case with the hook fractures that occurred with the EVT device, which were promptly disclosed. A public announcement was made, the details were published widely to surgeons,[1] and the trial was stopped and not resumed until the Food and Drug Administration was satisfied that reengineering had solved the problem.

When fabrication flaws were detected in another commonly used device, the Min Tec Stentor graft, some of us learned of disappearing (breaking) sutures from leaked discussions at investigator meetings well over a year before public acknowledgment came at meetings or, finally, in a publication.[2] This European report of seven explanted Stentor endografts showing "17-40% of the (polypropylene) ligatures of the body middle ring to be loose" and six of the seven with breakage, dislocation, endoleak, or occlusion was not published until this January. Just 2 months before this report was published, a presentation of the Eurostar data[3] reported a late endoleak rate of 2% to 10% per 6-month interval and the observation that "breakage of polypropylene sutures connecting the rings of the metal stent frame has *recently* been observed in one of the commercially available types of endografts." The device was pointedly *not* identified in the syllabus or presentation, purportedly because of an understanding with those funding the Eurostar registry that the data not be stratified and identified by specific device when presented and published by those running the registry. It was also noted in this presentation that a prospective study of 98 patients with this device at nine institutions showed breakage of multiple sutures in 37%. Five percent of the patients studied had endoleaks develop. Without presenting the details of the analysis that allowed them to draw their conclusions, the authors made the following cautious statements "… there was no correlation between suture breakage and the degree of angulation of the device (and) … no correlation … between device related endoleaks (and) suture

breakage." Other slightly earlier reports contained such statements as "no adverse events have been attributable to this observation" and "the clinical significance of this observation is unknown."

Min Tec's Stentor device has, of course, been taken over by Boston Scientific Corporation and has been superseded by the similar, but redesigned and differently fabricated, Vanguard device. So, one might assume that the suture breakage problem has been solved. In this issue, a case of a Vanguard graft has been reported[4] in which "a periprosthetic leak caused by a tear in the polyester prosthesis appeared between 9 and 12 months after surgery." The tear appeared adjacent to a suture breakage, causing separation of two struts of the nitinol wire framework in the body of the stentgraft. In this article, the authors point out "In this device, the metal components can move freely related to the covering fabric. When the sutures break, there might be a risk that the apex of a zigzag stent could angle into the fabric and cause focal wear." Later in the discussion, they point out that "According to the manufacturer of this device, suture breakage with separation of metal components is commonly seen, but perforation of the polyester prosthesis caused by movement of the metal stent against the fabric has not been reported." However, in an addendum to the revised manuscript they state "In November 1998, after this manuscript was prepared, we received an important message from Boston Scientific Corporation sent to all customers. Apparently, late endoleaks caused by holes in the fabric covering now have been reported to the manufacturer in six cases, and 'Investigations show that the failures are due to focal wear at the apex of a nitinol stent "zig" against the graft fabric.'" Other significant statements in this letter not included in this article are: "The reported events occurred between five and twelve months post-implant (which) suggests that the incidence will (not) increase with time" and "only one of the events described in this letter occurred within the Eurostar data set." However, five of these six cases were discussed by Dr Hugh G. Beebe when presenting an update on the United States Vanguard Endograft Trial at a breakfast session at the Montefiore Symposium last November. This may yet be simply a new and relatively low frequency form of endoleak with this device. However, subsequently the Safety Committee of the Dutch Society for Vascular Surgery has advised its members to stop implanting this device, although the appropriate action is, at this writing, still under consideration by a safety committee. The fact that this author was able to piece together most of the additional information included above by attending certain meetings and making personal contacts does not diminish the awareness gap that exists for much of the vascular community.

The issue of early if not immediate disclosure of possible device failures remains an important one. How else can investigators be certain that it is safe and ethical to continue the trial, and how else can practicing surgeons be sure that it is safe to refer their patients with AAAs for implantation of a particular endograft or, if they have appropriate endovascular skills, begin using a device that is being marketed? The entire issue of the control of clinical trials and their data by industry deserves scrutiny and will be the subject of another editorial in this journal.

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Please see the related article by Krohg-Sørensen et al on pages 1152-8.